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PERIPHERAL MECHANISMS IN CONGESTIVE HEART FAILURE

Classical interpretations of the cause of congestion and edema associated with heart failure have laid emphasis on the role of "backward" failure of the heart. The inability of the heart to pump efficiently has been considered to be the cause of stagnation and accumulation of blood behind the heart, resulting in elevation of venous pressure and eventual edema formation. More recently emphasis has shifted to the importance of "forward" failure resulting from impaired cardiac output as the basis of these disturbances. Principal organs affected by the impaired blood flow are the kidney, liver, and possibly certain endocrine organs. Modified function of these may then be the cause of impaired electrolyte and water metabolism, thus contributing to edema and congestion.

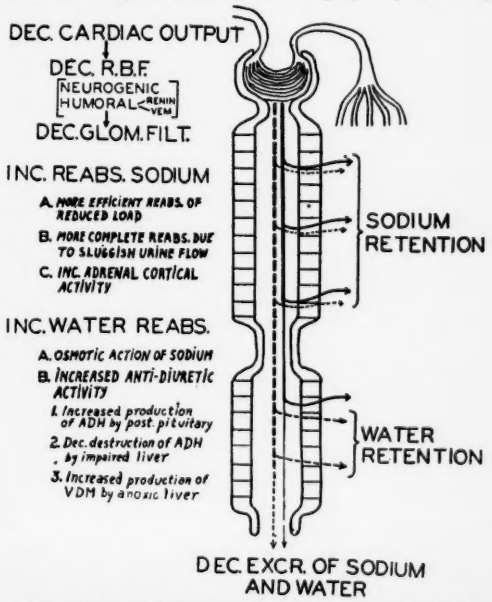
Consideration of left heart failure as a backward mechanism appears to give ready explanation for some of the striking symptoms noted: pulmonary congestion and edema with reduction in vital capacity, dyspnea, cough, and elevated pulmonary artery pressure. If heart failure is severe, the right ventricle is supposed to be involved, with elevation of right atrial pressure and eventually increase in peripheral venous pressure. In order to account for the pulmonary congestion, the question may logically be raised: where does the extra blood come from? This question becomes more pertinent when one considers in addition the extra blood needed to fill the peripheral venous bed.

Several possible sources of the extra blood have been considered. Arterial vasoconstriction, in response to decreased cardiac output, could cause a shift of blood to the venous circulation, but such a mechanism could probably not supply much. The possibility of venoconstriction has been brought forward by some as an explanation of the elevated venous pressure and a mechanism whereby blood could be shifted from reservoir organs to the central veins. However, reflex changes by which such mechanisms would operate have not been well defined. A third important alternative is that a sequence of events is put into play which results in increase in blood volume.

Evidence is ample that blood volume is increased in congestive heart failure by about 25 per cent greater than normal both by T-1824 and tagged erythrocyte methods. The increase in plasma volume is a manifestation of a similar increase in total extracellular volume, as evidenced by increase in thiocyanate space. The increase in interstitial fluid volume is the basis of the concurrent edema.

This leads to a consideration of the mechanism of edema formation in congestive heart failure. If one considers first the possible consequences of backward failure and elevated venous pressure, simple filtration of fluid should immediately result in a *decrease* in blood volume and hemoconcentration, contrary to the experimental findings. Furthermore, permanent deviation of fluid to the interstitial compartment should prove difficult in the presence of normal lymphatic function. Thus, Burch and Winsor[1] found that after ligation of the inferior vena cava below the renal veins in five patients that edema of the extremities followed immediately but usually subsided to variable degrees. In one instance no edema was present with a venous pressure as high as 50 cm. of water. The soundest explanation for increase in extracellular fluid volume would be one that would account for water retention and a parallel retention of sodium salt as the necessary osmotically active ingredient. One therefore logically searches for renal dysfunction to explain the mechanism of edema formation.

The renal alterations which serve as a basis for salt and water retention are largely explained by



Schematic presentation of current views of the mechanism for salt and water retention by the kidney. Solid arrows to the right denote sodium reabsorption, broken arrows, water reabsorption.

changes which are consequent on "forward" failure because of reduced cardiac output and impaired circulation. Merrill[2] has demonstrated that cardiac output is usually below the normal mean. However, since edema is noted in "high output" failure, the mechanism is set into play not so much by the absolute level of cardiac output, but rather as emphasized by Little[3] by the relation of: $\frac{\text{oxygen supply}}{\text{oxygen consumption}}$, a ratio which he terms the "oxygen index." This averages about 4.65 in normal individuals and only about 2.5 in congestive failure. For example, in anemia the numerator is reduced, and in thyrotoxicosis the denominator increases.

The reduction in cardiac output is considered to be the direct cause of the reduced renal function which is associated with congestive heart failure. This is manifested by the large reduction in renal plasma flow to ⅓ to ⅕ of normal. The cause of the reduction in renal blood flow may be on a neurogenic reflex basis or on a humoral basis. Evidence of increased renin and VEM (vaso-excitor material) production has been brought forward. Renin, which produces hypertensin (angiotonin), and VEM both could favor further reduction in renal blood flow. Concomitantly, glomerular filtration rate is reduced to about one-half of normal.

Evidence is now abundant that decreased excretion of sodium occurs during decompensation, and that its excretion increases during compensation. As Merrill has pointed out, normally 1.23 per cent of the filtered sodium is excreted. This may drop to one-half or less in cardiacs. According to this writer, sodium retention is the result of decrease in sodium load to the tubular reabsorptive mechanism resulting from the decrease in glomerular filtration rate, and a more efficient reabsorption of the reduced load by unimpaired tubular sodium transfer systems. Marked reduction in sodium excretion indeed occurs in animals when glomerular filtration is experimentally reduced under conditions which control other possible factors[4]. Another hemodynamic variable which may directly influence sodium retention is the renal venous pressure. Experimental elevation of renal venous pressure in man and dog has been shown to favor sodium retention[5,6]. A tentative explanation is that venous congestion tends to compress certain portions of the renal tubule by distended renal vein radicles; this may slow the movement of urine and favor more complete reabsorption of sodium and water.

Although the importance of the glomerulo-tubular imbalance in sodium reabsorption is recognized, several investigators have found no correlation between glomerular filtration rate and decompensation and compensation in congestive failure. These findings suggest that other factors which bear directly on the renal tubular reactivity to salt and water may be operative in the cardiac patient. These are humoral factors which influence salt and water reabsorption.

Evidence of increased adrenal cortical activity in congestive patients is offered by the frequent finding of low sweat sodium. Parrish[7] has found increased adrenal corticoid excretion by bio-assay methods in the urine of patients ill with congestive heart failure. The suggestion has been made that impaired blood supply and anoxia constitute a type of "alarm reaction" which promotes increased output of the adrenal electrolyte retaining hormones. On the other hand, there is ample evidence that liver impairment coexists, and it may well be that the increased presence of cortical hormones may be the result of impairment of the normal metabolic alteration by the liver.

Hepatic impairment as a sequel to congestive heart failure is worthy of further emphasis. Clinical symptoms of swollen liver and slight jaundice are common. Liver cells become swollen and engorged, and cells are destroyed. In an advanced stage, this leads to "cardiac cirrhosis"[8] and may contribute to the development of ascites. Reduced cardiac output and impaired hepatic blood flow and anoxia are basic for the impairment. Hepatic blood flow has been found to be reduced to about 60 per cent of normal by the bromsulphalein method[9].

Evidence of specific water retention suggests that antidiuretic substances circulate in increased amounts. Increased amounts of antidiuretic substance have been recovered in the urine of congestive patients[10]. This may result either from some specific stimulus to the neurohypophysis with increased release of ADH, or, again, from decreased destruction by the impaired liver. VDM has been found in increased amounts in the hepatic vein blood of congestive patients[11], and has been shown to have an antidiuretic action. Latest work suggests that it does this by stimulating the neurohypophysis which in turn elaborates increased amounts of ADH.

The main factors which may act on the kidney to favor salt and water retention are illustrated in the accompanying figure. It emphasizes that no single factor may alone be responsible for salt and water retention, and illustrates why in the treatment of the edema of heart failure one regime may be more successful than another.

In summary of the interrelation of factors concerned in congestive heart failure it appears that certain aspects of backward and forward failure complement each other to best explain the final picture. Thus, elevated venous pressure favors the movement of fluid and salt into the interstitial spaces. This results in reduction of blood volume which contributes to the reduced cardiac output of forward failure. This in turn favors salt and water retention by the kidney to provide a mechanism to explain hypervolemia and increase in extracellular volume. Hypervolemia further increases the venous pressure, so that the cycle is repeated resulting in a net increase in interstitial volume and circulating plasma volume. Furthermore, increase in erythrocyte volume results from stimulation of the bone marrow by anoxia.

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